
Simultaneous deletion of NOD1 and NOD2 inhibits in vitro alloresponses but does not prevent allograft rejection.

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Public Summary:

Pattern recognition receptors (PRRs) play an important role in host anti-donor responses to transplanted tissue. A key trigger of the host alloresponse involves recognition of foreign antigen presented on activated antigen presenting cells by the host T cells. Emerging data suggest that PRR blockade can abrogate host anti-donor responses by interfering with activation of antigen presenting cells, particularly activation of dendritic cells. Our study asked whether blockade of a well-characterized family of intracellular PRRs, the NOD family, interfered with alloantigen recognition and allograft rejection. We found that deletion of either NOD1 or NOD2 in antigen presenting cells (APCs) had no effect on induction of T cell proliferation to alloantigen, but that simultaneous deletion of NOD1 and NOD2 significantly inhibited T cell responses. There was however no effect of the NOD deletion on skin graft rejection when NOD1xNOD2 skin was transplanted onto allogeneic hosts or when WT skin was transplanted onto NOD1xNOD2 deficient recipients. The conclusion of this study is that in vitro alloresponses are negatively impacted by the simultaneous deletion of NOD1 and NOD2, but that allograft rejection across a stringent allo barrier is not affected. Our results suggest that the NOD family members, NOD1 and NOD2, play a collaborative role in T cell activation by alloantigen and that their blockade in vitro can inhibit T cell responses.

Scientific Abstract:

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